Promoter CpG methylation contributes to ES cell gene regulation in parallel with Oct4/Nanog, PcG complex, and histone H3 K4/K27 trimethylation.

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Public Summary:

Scientific Abstract:
We report here genome-wide mapping of DNA methylation patterns at proximal promoter regions in mouse embryonic stem (mES) cells. Most methylated genes are differentiation associated and repressed in mES cells. By contrast, the unmethylated gene set includes many housekeeping and pluripotency genes. By crossreferencing methylation patterns to genome-wide mapping of histone H3 lysine (K) 4/27 trimethylation and binding of Oct4, Nanog, and Polycomb proteins on gene promoters, we found that promoter DNA methylation is the only marker of this group present on approximately 30% of genes, many of which are silenced in mES cells. In demethylated mutant mES cells, we saw upregulation of a subset of X-linked genes and developmental genes that are methylated in wild-type mES cells, but lack either H3K4 and H3K27 trimethylation or association with Polycomb, Oct4, or Nanog. Our data suggest that in mES cells promoter methylation represents a unique epigenetic program that complements other regulatory mechanisms to ensure appropriate gene expression.